Centers for Disease Control and Prevention Initiatives to Prevent Hepatitis C Virus Infection: A Selective Update

Bryce D. Smith, Cynthia Jorgensen, Jon E. Zibbell, and Geoff A. Beckett
Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia

Hepatitis C virus (HCV) infection is a complex public health problem, characterized by a high prevalence of chronic infection, an increasing burden of HCV-associated disease, low rates of testing and treatment, and the prospect of increasing incidence associated with the epidemic of injection drug use. Three-quarters of chronic HCV infections occur among persons born from 1945 through 1965. Prevention efforts are complicated by limited knowledge among health care professionals, persons at risk and in the public at large. At the Centers for Disease Control and Prevention, efforts to improve primary and secondary prevention effectiveness center on policy development, education and training initiatives, and applied research. This report provides a brief overview of some of these efforts, including the development of testing recommendations for the 1945–1965 birth cohort, research and evaluation studies in settings where persons who inject drugs receive services, and a national viral hepatitis education campaign that targets health care professionals, the public, and persons at risk.

In the United States, an estimated 3.2 million persons are infected with hepatitis C virus (HCV) [1]. HCV-associated liver disease is the leading indication for liver transplantation, and chronic HCV infection is a leading cause of hepatocellular carcinoma [2–4]. In 2007, HCV infection caused more deaths than human immunodeficiency virus (HIV) infection in the United States [5]. Morbidity and mortality attributable to HCV infection is projected to increase dramatically over the next 40–50 years such that, without treatment, 1.76 million persons will develop cirrhosis, 400 000 will develop hepatocellular carcinoma, and approximately 1 million will die from HCV-associated complications [6]. Incident cases of HCV infection also continue to add to the disease burden; of the 16 000 persons who were newly infected with HCV in 2009, the Centers for Disease Control and Prevention (CDC) estimates that 75%–85% (12 000–13 600) will develop chronic HCV infection [7]. Transmission associated with injection drug use (IDU) continues to be the leading risk for new infections with HCV [8].

Most persons who are positive for HCV antibody (anti-HCV) [9–11] are believed to be unaware of their HCV status because they have not been tested and/or informed of their test results; low rates of testing and diagnosis result in missed opportunities for medical evaluation, care, and treatment, as well as for counseling to promote behavioral changes that might reduce disease progression and avert transmission of infection. There is also evidence that many HCV-infected persons in care who have been tested and received a diagnosis are not referred for evaluation and possible treatment by a specialist and do not receive other recommended clinical services. Recent Food and Drug Administration–approved direct-acting antivirals (DAAs) [12, 13] have increased HCV infection cure rates, and therefore improved diagnosis and linkage to care and treatment have become increasingly important.

HCV prevention strategies at the CDC Division of Viral Hepatitis include primary and secondary
prehension approaches that have been framed by the Action Plan for the Prevention, Care and Treatment of Viral Hepatitis, issued by the US Department of Health and Human Services in 2011 [14]. Presented here is a brief summary of selected CDC prevention initiatives that address 3 problem areas: (1) high HCV prevalence in the 1945–1965 US birth cohort, (2) low levels of public and professional awareness, and (3) high HCV infection incidence associated with the epidemic of IDU.

THE HIGH PREVALENCE OF HCV INFECTION IN THE 1945–1965 BIRTH COHORT

The CDC estimates that the overall prevalence of HCV infection is the United States is approximately 1.6%, with significant variations in prevalence seen across many demographic subpopulations. During the 1990s, epidemiologists first observed disproportionately higher HCV infection rates among persons who were born during the post–World War II baby boom, from the mid-1940s through the mid-1960s [14]. An analysis of National Health and Nutrition Examination Survey (NHANES) data from 1999–2002 showed that 65.6% of all persons with HCV antibody were born between 1945 and 1964 [1]. Similarly, in an analysis of 1988–1994 NHANES data, 65% of persons with HCV antibody were 30–49 years old (representing birth years 1939–1963) when the surveys were conducted [15].

Epidemiological modeling has indicated that the incidence of HCV infection rose significantly in the late 1960s and continued to be very high before sharply decreasing after 1989 [16]. The high prevalence of HCV infection among persons born from 1945 through 1965 is largely attributed to exposures that occurred during this period of increased incidence, and many of those exposures were associated with IDU or blood transfusion [1, 17].

The CDC Division of Viral Hepatitis has recently completed an analysis of NHANES data for surveys conducted during 1999–2008. From this data, the CDC estimates that three-quarters of all persons currently living with chronic HCV infections are in the 1945–1965 birth cohort [18], a population that in 2012 includes persons aged 47–67 years. The HCV infection prevalence in this cohort is 3.29%, which represents approximately 2 million persons and is 5 times the prevalence among persons born outside the birth cohort (0.55%) [18].

ADDRESSING THE HIGH BURDEN OF HCV INFECTION IN THE 1945–1965 BIRTH COHORT

Given the high HCV infection prevalence in the 1945–1965 birth cohort, it is not surprising that >70% of deaths among HCV-infected persons occurred in this age group in 2007 [5]. Rapidly increasing HCV-related morbidity and mortality are expected to have a significant impact on this birth cohort, as 61% of all HCV-infected persons are forecasted to develop cirrhosis, and 37% are expected to die from liver disease [6]. Further, studies estimate that 45%–85% of HCV-infected persons are unaware of their status [9–11]. Without knowledge of their status, infected persons cannot avail themselves of the recent availability of DAAs that dramatically increase the effectiveness of therapy [12, 13]. Last, testing for and treatment of HCV infection in the 1945–1965 birth cohort, when compared with current risk-based testing and treatment, has been determined to be cost-effective at $15 700 per quality-adjusted life year (QALY) on the basis of a regimen of pegylated interferon with ribavirin and increases to $35 700 per QALY when more effective yet more expensive DAAs are added to the regimen. This cost analysis also forecasts that between 80 000 and 120 000 lives could be saved with the implementation of birth cohort testing as compared to current risk-based testing [17].

The CDC is responding to these findings by considering a recommendation for 1-time HCV testing for all persons born during 1945–1965 and subsequent linkage to care and treatment as appropriate. In 2011, the CDC conducted an evidence-based review of the literature related to HCV infection prevalence in the birth cohort, as well as patient-important outcomes related to HCV testing and treatment, using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method [19]. A proposed birth cohort testing recommendation has been drafted and is currently under consideration. The CDC is beginning to plan for implementation of the proposal, as well as for evaluation of its implementation and adoption, if it becomes a formal recommendation.

HCV KNOWLEDGE AND AWARENESS

Low levels of awareness and knowledge about HCV have been identified as a formidable challenge to prevention and care [20]. Many healthcare professionals lack basic knowledge about risk factors or screening recommendations associated with viral hepatitis. Several studies have documented limited physician knowledge about HCV prevalence and natural history [20–22], and fewer than half of all physicians in the United States ask their patients sensitive questions related to high-risk behaviors, such as IDU [21]. Knowledge about HCV is also limited in the general public. In the 2010 HealthStyles, a consumer marketing survey of 4071 participants, 41% of respondents disagreed with the statement, “I am knowledgeable about viral hepatitis,” and an additional 30% had a neutral opinion [14, CDC, HealthStyles survey report, November 2010].
This finding was supported and amplified in CDC-sponsored focus groups, in which misconceptions about viral hepatitis were common [CDC, unpublished data, December 2011]. Many participants assumed that they were tested for hepatitis when blood tests were performed, as part of their routine physical examinations. In addition, some focus group participants believed that if they were infected they would have symptoms, and others concluded that the virus could not be detected in their blood if they were asymptomatically infected.

THE KNOW MORE HEPATITIS NATIONAL HEPATITIS EDUCATION CAMPAIGN

The CDC Division of Viral Hepatitis is developing the Know More Hepatitis National Education Campaign, which will be launched in 2012. The goals of the campaign are to raise awareness about viral hepatitis, change perceptions associated with the disease, and increase the identification of people who are currently unaware of their chronic HCV infection and link them to treatment. The campaign is designed to complement existing hepatitis prevention efforts, leverage the CDC’s credibility and expertise, capitalize on the CDC’s network of state and local partners, and enhance public-private partnerships. The campaign is scientifically based and rooted in behavioral change theory and consists of 3 distinct, overlapping phases, each targeting specific audiences. The campaign is following a rigorous formative research and testing process designed to maximize the potential effectiveness of the messages, and will use multimedia strategies, including print, broadcast, digital, and social media.

Phase I of the campaign is designed to place viral hepatitis on the national agenda and to raise its importance as an urgent public health issue among policy makers, opinion leaders, healthcare professionals, and the general public. To this end, the campaign was announced in 2011 at a White House event on World Hepatitis Day, featuring a presidential proclamation on viral hepatitis. The CDC has used media advocacy and social media strategies during this phase to stimulate discussion about viral hepatitis. Phase I is designed to continue throughout the duration of the Know More Hepatitis campaign, adapting messages to reflect the current news environment and upcoming guidelines.

Phase II of the Know More Hepatitis campaign focuses on healthcare professionals and will address perceived and real barriers to screening. By using findings from the CDC’s formative research with primary care professionals, strategies will include educational components designed to increase knowledge about chronic viral hepatitis and to build health care professionals’ capacity to conduct risk assessments and test patients at risk. If professionals are knowledgeable and comfortable with screening, testing of patients at risk may increase. More importantly, professionals will be prepared as patients respond to the direct-to-consumer part of the campaign, which encourages patients to be aware of their risk, talk with their physicians, and get tested. The launch of the second phase will be in conjunction with the release of the CDC’s birth cohort HCV testing recommendation, anticipated to be in 2012.

The CDC will launch phase III, the third and final phase of the national campaign, in conjunction with Hepatitis Awareness Month in May 2012. A combination of strategies will be used to disseminate the message, including print and broadcast media, online tools, and social media. This phase will target the same groups specified in the CDC’s expanded guidelines for HCV testing. Another major component of this phase will be activities to promote National Viral Hepatitis Testing Day on 19 May. The CDC is developing an interactive risk assessment tool designed to determine an individual’s risk for viral hepatitis. The tool asks questions based on CDC’s guidelines for testing and vaccination for viral hepatitis and allows individuals to privately answer questions in either their home or in a healthcare setting. Once the assessment is completed, individualized recommendations for testing and/or vaccination will be produced, which can be printed and shared with a healthcare professional.

HCV INFECTION AMONG PERSONS WHO INJECT DRUGS (PWID): BACKGROUND

IDU continues to be the leading risk factor for HCV incidence in the United States, and PWID have the highest prevalence of HCV infection of any population, ranging from 40%–70% in most studies [23–27]. Public health strategies to reduce the burden of IDU-associated HCV infection include primary and secondary prevention efforts and improvements in linkage of infected PWID to care and treatment services [14].

There is increasing evidence that multicomponent programs, which provide a combination of substance abuse treatment and support for safe injection practices that decrease the shared use of injection equipment, are most likely to be effective in preventing new HCV infections among PWID. There is a critical need for research and program evaluation to determine the best designs for these interventions [14]. Because the highest incidence rates of HCV infection occur in persons who recently initiate IDU, primary prevention interventions must be able to reach new injectors and noninjectors who are at risk of initiating IDU [26, 28, 29]. As heroin injection and the illicit use of prescription opiates are increasing in the United States, IDU-associated HCV infection may be increasing in some areas, especially among adolescents and young adults. Efforts to identify and provide prevention services to young PWID and to users of noninjection drugs who may transition to IDU are critical [30, 31].
HCV testing rates among PWID are low, and many HCV-infected PWID are unaware of their infection status; knowledge about HCV infection may be low among drug addiction treatment staff, and HCV educational resources for PWID receiving services are underused in drug treatment programs [32–34]. Because >90% of PWID who receive a diagnosis of acute HCV infection have a history of incarceration or previous drug treatment at the time of diagnosis, both correctional facilities and drug treatment programs provide important opportunities for primary prevention efforts, testing, and care associated with HCV infection [27].

**HCV INFECTION PREVENTION FOR PWID: CDC ACTIVITIES**

At the CDC, there has been considerable expansion of the research agenda for HCV infection prevention issues related to PWID over the past 2 years. The Division of Viral Hepatitis has been actively involved in research and evaluation of anti-HCV rapid tests in laboratory and field settings [35, 36]. One HCV rapid test was approved for the US market by the Food and Drug Administration in June 2011 and was granted a Clinical Laboratory Improvement Amendment waiver for use in nonlaboratory settings. The CDC expects HCV rapid tests to become a significant tool in providing point-of-care test results to PWID, a population that has significantly limited access to healthcare services and may be lost to follow-up if immediate test results are not available.

The CDC and research partners are currently planning a study aimed at providing clinical management and prevention services to persons with HCV infection who are participating in opiate substitution treatment yet still engaging in high-risk activities (ie, drug use). In addition to receiving disease- and treatment-related education, participants can receive a medical evaluation for possible HCV therapy and can enroll in prevention services, such as individual and group behavioral interventions.

The CDC Division of Viral Hepatitis is also exploring community-level interventions and the feasibility of using structural interventions at syringe services programs to reach this underserved and often hidden population. Prevention strategies that can reach neophyte injectors before they become infected must include development of effective techniques for PWID to discontinue IDU and ways to avoid high-risk practices for those unable to cease IDU. Syringe services programs are the most capable of reaching this population, and their focus on harm reduction education creates an ideal setting to design and field-test education interventions meant to reduce the transmission of HCV associated with IDU. Development of partnerships for research and evaluation with community-based organizations and health departments providing prevention services is a CDC priority.

**CONCLUSION**

The CDC is pursuing multiple HCV infection prevention efforts to reduce the disease burden and incident infection in parallel with a broad education campaign targeting both professionals and consumers. Primary prevention strategies center on efforts to reach more PWID, in settings where they receive services, such as drug treatment and syringe services programs. Secondary prevention initiatives are intended to increase HCV testing to identify the large numbers of persons with undiagnosed and untreated chronic HCV infection and to help ensure that they are linked to appropriate and effective care. In 2012, the CDC will continue its systematic review of HCV screening and testing recommendations and will issue updated guidance when this review is completed. The identification and implementation of effective models of HCV care is a necessary complement to enhanced screening policies, and the CDC will be working closely with its sister health agencies and with medical societies, clinical researchers, payors, and other health policy makers in these efforts, as well.

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